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February 15, 2005

Division of Dockets Management
Food and Drug Administration (HFA-305)
Department of Health and Human Services
5630 Fishers Lane, Room 1061
Rockville, MD 20852

CITIZEN PETITION

Dear Sir or Madam:

The undersigned submits this petition, in quadruplicate, pursuant to Section 505(j)(2)(C) of the Federal Food, Drug and Cosmetic Act and in accordance with 21 CFR 10.30 requesting the Commissioner of the Food and Drug Administration declare the drug product, Chlorhexidine Gluconate 2% w/v and Isopropyl Alcohol 70% v/v Patient Preoperative Skin Preparation 3 mL, in a different dosage form suitable for consideration as an abbreviated new drug application (ANDA).

A. Action Requested

The petitioner requests the Commissioner of the Food and Drug Administration declare the drug product Chlorhexidine Gluconate 2% w/v and Isopropyl Alcohol 70% v/v Patient Preoperative Skin Preparation 3 mL suitable for submission in an ANDA. The petitioner seeks a change to the dosage form from that of the reference listed drug product. This petition is based on the reference listed drug (RLD) ChloraPrep® (Chlorhexidine Gluconate 2% w/v and Isopropyl Alcohol 70% v/v Patient Preoperative Skin Preparation) indicated for the preparation of the skin prior to surgery. Medi-Flex, Inc. is the sponsor of the RLD under NDA 20-832 and marketing exclusivity expired July 14, 2003. A copy of the listing from the Electronic Orange Book (http://www.fda.gov/cder/ob/default.htm) is included in Attachment 1.

B. Statement of Grounds

The RLD is currently available in product volumes of 1.5 mL, 3 mL, and 10.5 mL. Aplicare proposes to submit an ANDA for the 3.0 mL product using a modified applicator. Therefore, only the 3.0 mL dosage form is discussed in this petition. The approved 3.0 mL product consists of a dry polyurethane foam sponge applicator located on the end of a plastic applicator handle with wings. The drug product solution is contained within a sealed glass ampule located inside the applicator handle. Pinching the wings of the handle breaks the ampule and saturates the foam sponge. The drug product is applied directly to the skin via the foam sponge to prepare the skin for surgery in accord with the labeled directions.

The petitioner seeks to submit an ANDA for a 3.0 mL product using presaturated sponges on the end of plastic applicator handles. As the sponges of the proposed product would be presaturated, the user simply opens the package and applies the antiseptic directly to the skin without having to break a glass ampule in preparation for skin application. Three (3) presaturated applicators saturated with a total volume of 3.0 mL of the solution would be packaged within one (1) foil pouch. The foam sponge material used to apply the drug product would be identical to the RLD sponge material for the 3 mL dosage form; i.e., 100 PPI white polyurethane foam. Therefore, the user would administer the drug

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product from all three sponge foam applicators in accord with the method of use identical to that of the RLD (apply saturated foam sponge containing the drug product directly to skin in accord with labeled directions), using the identical foam material.

To illustrate the approved 3.0 mL RLD product as well as the proposed product, the following images are provided. Image #1 is a rendering of the RLD obtained from the Medi-Flex, Inc. web site (www.medi-flex.com); Image #2 is a photograph of the RLD (right) and the proposed product (left).

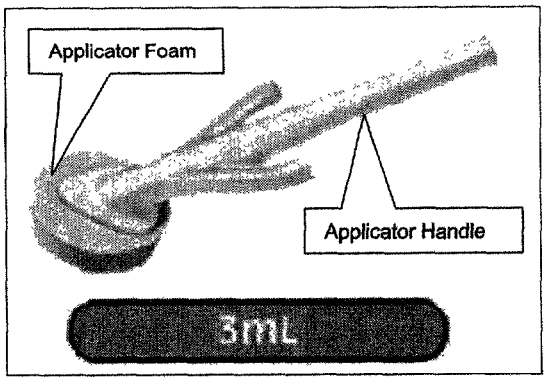


Image #1 – rendering of RLD

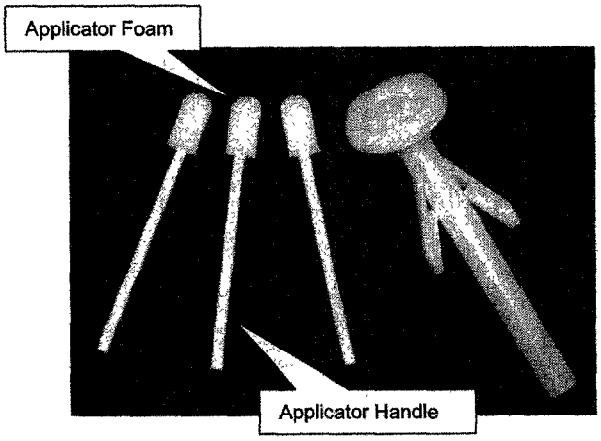


Image #2 – Photo of proposed product (left) and RLD (right)

The proposed change from an applicator requiring the user to saturate the foam sponge prior to use to presaturated sponges requires minimal changes to the product labeling. The following table outlines the current RLD product Directions for Use of the 3 mL dosage form (see Attachment 2) and the proposed changes:

Directions for Use	
3 mL ChloraPrep®	**3 mL Proposed Drug Product**
▪ Pinch the wings on the applicator to break the ampule and release the antiseptic. Do not touch the sponge. Wet the sponge by repeatedly pressing and releasing the sponge against the treatment area until liquid is visible on the skin.	▪ Open package at tear notch. ***Change: Statement revised as it does not apply to presaturated sponges.***
▪ ***dry surgical sites*** (such as abdomen or arm): Use repeated back-and-forth strokes of the sponge for approximately ***30 seconds***. Completely wet the treatment area with antiseptic. Allow the area to air dry for approximately 30 seconds. Do not blot or wipe away.	▪ ***dry surgical sites*** (such as abdomen or arm): Use repeated back-and-forth strokes of the sponges for approximately ***30 seconds***. Completely wet the treatment area with antiseptic. Allow the area to air dry for approximately 30 seconds. Do not blot or wipe away. ***Changes: Add "s" to make sponge plural.***

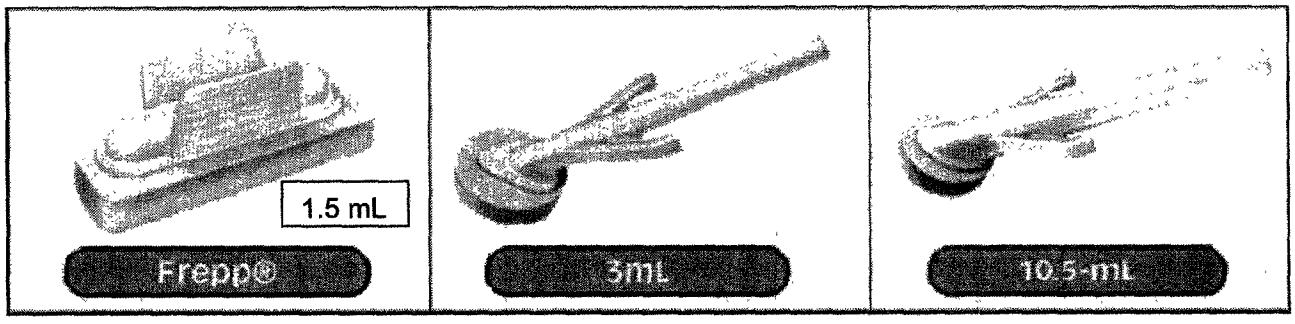
Directions for Use (Continued)	
3 mL ChloraPrep®	**3 mL Proposed Drug Product**
■ **moist surgical sites** (such as the inguinal fold): Use repeated back-and-forth strokes of the sponge for approximately ***2 minutes***. Completely wet the treatment area with antiseptic. Allow the area to air dry for approximately one (1) minute. Do not blot or wipe away.	■ **moist surgical sites** (such as the inguinal fold): Use repeated back-and-forth strokes of the sponges for approximately ***2 minutes***. Completely wet the treatment area with antiseptic. Allow the area to air dry for approximately one (1) minute. Do not blot or wipe away. ***Changes: Add "s" to make sponge plural.***
■ maximum treatment area for one applicator is approximately 130 cm^2 (approx. 4 X 5 in.). Discard the applicator after a single use.	■ maximum treatment area for one application is approximately 130 cm^2 (approx. 4 X 5 in.). Discard the applicator after a single use. ***Changes: "Applicator" changed to "Application" to reflect the use of three sponges in proposed package.***

All other text on the labeling remains identical and no other changes are proposed; **the drug product formulation would be identical to the RLD in regard to both the active and inactive ingredients**.

The following table summarizes the physical and chemical similarities and differences between the 3 mL RLD and the proposed product.

	RLD	Proposed Product
Active Ingredients	Chlorhexidine Gluconate (CHG) Isopropyl Alcohol (IPA)	Chlorhexidine Gluconate (CHG) Isopropyl Alcohol (IPA)
Inactive Ingredients	Purified water	Purified water
Strength	2% CHG (w/v) 70% IPA (v/v)	2% CHG (w/v) 70% IPA (v/v)
Dosage Form	Liquid	Liquid
Route of Administration	Topical	Topical
Volume	3.0 mL (approx.)	3.0 mL (approx.)
Applicator Foam	100 PPI white polyurethane foam sponge	100 PPI white polyurethane foam sponge
Applicator handle length	4.5" (approx)	4" (approx)
Surface area of applicator	1.75 sq. in. circle (approx.)	3.0 sq. in. (approx; 1.0 sq. in. per each of 3 swabsticks)
Packaging / drug contact surface	Inert glass	Inert plastics in a foil based laminate.
# Applicator devices / product	One	Three

The petitioner notes that the RLD has been approved with three (3) separate dosage form configurations (see below) consisting of sponge materials (differing in material, density, and surface area), attached to plastic handles of different dimensions, delivering different amounts of the same drug substance. By virtue of each of the three (3) dosage form configurations being approved, it is evident that efficacy was sufficiently demonstrated in each. Thus, within the limits of the three (3) dosage form configurations approved, a robustness of the RLD antiseptic's efficacy, independent of the dosage form dimensions or the material used to apply the antiseptic to the skin, is evident. As noted in the table above, the composition and amount of antiseptic formulation and the composition of the foam material provided with the proposed product would be identical to that of the 3 mL RLD (i.e., the same drug product would be applied using the same sponge material); the surface area of the proposed product's foam sponge material would be greater than the 3 mL RLD applicator, but approximately the same as the approved 1.5 mL RLD applicator (approx. 3 in^2 vs. 2.66 in^2 respectfully).



The petitioner also notes that the proposed presaturated sponges as outlined above are safer to use. The RLD product solution is contained within a glass ampule that must be broken by the user prior to administration. Resulting injury from glass shards on similar products have been reported via MedWatch reports to the Agency (see Attachment 3). The proposed product does not contain any glass components and is safer from this perspective. Similarly, because the proposed product consists of three presaturated sponges packaged in a laminated foil/plastic pouch, breakage during shipment or handling, especially at low temperatures, is not a concern.

Copies of labels of the reference-listed drug product upon which this petition is based and draft labels for the proposed product are included as Attachment 2 and Attachment 4, respectively.

Therefore, the petitioner requests that the Commissioner find the requested change in dosage form equivalent to the RLD because the change does not raise issues of safety or effectiveness. The Agency should approve this petition to allow submission of an ANDA for the proposed dosage form.

C. Environmental Impact
The petitioner claims a categorical exclusion under 21 CFR 25.31.

D. Economic Impact
The petitioner believes that an economic impact assessment is not applicable for this petition, but agrees to provide such an analysis if requested by the Commissioner.

E. Certification

The undersigned certifies that to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioner, which are unfavorable to the petition.

Respectfully submitted,

Greg Art

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Attachments:
1. Copy of Electronic Orange Book (http://www.fda.gov/cder/ob/default.htm) of the RLD under NDA 20-832
2. Copy of RLD label (including Directions for Use) upon which this petition is based
3. References to glass causing injury in devices similar to the RLD
4. Copies of labels of the proposed product

cc: Mr. Gary Buehler (OGD)